
Handbook of PHARMACEUTICAL EXCIPIENTS

Third Edition

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Albumin

1. Nonproprietary Names

BP: Albumin solution
PhEur: *Albumini humani* solutio
USP: Albumin human

2. Synonyms

Albuconn; albumin human solution; *Albuminar*; *Albuminol*; *Albuspan*; *Albutein*; *Buminate*; HSA; human serum albumin; normal human serum albumin; *Plasbumin*; plasma albumin; *Pro-Bumini*; *Proserum*.

3. Chemical Name and CAS Registry Number

Serum albumin [9048-49-1]

4. Empirical Formula Molecular Weight

Human serum albumin has a molecular weight of about 69 500 and is a single polypeptide chain consisting of 585 amino acids. Characteristic features are a single tryptophan residue, a relatively low content of methionine (6 residues), and a large number of cystine (17) and of charged amino acid residues of aspartic acid (36), glutamic acid (61), lysine (59), and arginine (23).

5. Structural Formula

Primary structure: Human albumin is a single polypeptide chain of 585 amino acids and contains 7 disulfide bridges.

Secondary structure: Human albumin is known to have a secondary structure that is about 55% α -helix. The remaining 45% is believed to be divided among turns, disordered, and β -structures.⁽¹⁾

Albumin is the only major plasma protein that does not contain carbohydrate constituents. Assays of crystalline albumin show less than one sugar residue per molecule.

6. Functional Category

Stabilizing agent; therapeutic agent.

7. Applications in Pharmaceutical Formulation or Technology

Albumin is primarily used as an excipient in parenteral pharmaceutical formulations where it is used as a stabilizing agent for formulations containing proteins and enzymes.⁽²⁾ Albumin has also been used to prepare microspheres and microcapsules for experimental drug-delivery systems.⁽³⁾

As a stabilizing agent, albumin has been employed in protein formulations at concentrations as low as 0.003% although concentrations of 1-5% are commonly used. Albumin has also been used as a cosolvent⁽⁴⁾ for parenteral drugs, as a cryoprotectant during lyophilization and to prevent adsorption of other proteins to surfaces.

Therapeutically, albumin solutions have been used parenterally for plasma volume replacement and to treat severe acute albumin loss. However, the benefits of using albumin in such

applications in critically ill patients has recently been questioned.⁽⁵⁾

8. Description

The USP describes albumin human as a sterile nonpyrogenic preparation of serum albumin obtained from healthy human donors, *see* Section 13. It is available as a solution containing either 4, 5, 20, or 25 g of serum albumin in 100 mL of solution, with not less than 96% of the total protein content as albumin. The solution contains no added antimicrobial preservative but may contain sodium acetyltryptophanate with or without sodium caprylate as a stabilizing agent.

The PhEur similarly describes albumin solution as an aqueous solution of protein obtained from human plasma, *see* Section 13. It is available as a concentrated solution containing 150 g/L to 250 g/L of total protein or as an isotonic solution containing 35 g/L to 50 g/L of total protein. Not less than 95% of the total protein content is albumin. A suitable stabilizer against the effects of heat, such as sodium caprylate (sodium octanoate) or *N*-acetyltryptophan or a combination of these two at a suitable concentration, may be added but no antimicrobial preservative is added.

Aqueous albumin solutions are slightly viscous and range in color from almost colorless to amber depending upon the protein concentration. In the solid state, albumin appears as brownish amorphous lumps, scales, or powder.

9. Pharmacopeial Specifications

Test	PhEur	USP
Character	+	—
Identification	+	—
pH (10 g/L solution)	6.7-7.3	+
Polymers and aggregates	+	—
Potassium	≤ 0.05 nmol/L	—
Sodium	≤ 160 mmol/L	130-160 mEq/L
Heavy	+	+
Albumin	≤ 200 μ g/L	—
Sterility	+	+
Hepatitis B surface antigen	—	+
Pyrogens	+	+
Total protein	95-105%	—
for 4 g in 100 mL	—	93.75-106.25%
for 5 to 25 g in 100 mL	—	94.0-106.0%
Total protein that is albumin	$\geq 95\%$	$\geq 96\%$
Protein composition	+	—
Prekallikrein activator	≤ 35 IU/mL	—

10. Typical Properties

Acidity/alkalinity: pH = 6.7-7.3 for a 1% w/v solution, in 0.9% w/v sodium chloride solution, at 20°C.

Osmolarity: a 4-5% w/v aqueous solution is iso-osmotic with serum.

Solubility: freely soluble in dilute salt solutions and water. Aqueous solutions containing 40% w/v albumin can be readily prepared at pH 7.4. The high net charge of the peptide contributes to its solubility in aqueous media. The seven disulfide bridges contribute to its chemical and spatial conformation. At physiological pH, albumin has a net electrostatic charge of about -17. Aqueous albumin solutions are slightly viscous and range in color from almost colorless to amber depending upon the protein concentration.

6 Albumin**11. Stability and Storage Conditions**

Albumin is a protein and therefore susceptible to chemical degradation and denaturation by exposure to extremes of pH, high salt concentrations, heat, enzymes, organic solvents, and other chemical agents.

Albumin solutions should be protected from light and stored at a temperature of 2-25°C or as indicated on the label.

12. Incompatibilities

See Section 11.

13. Method of Manufacture

Albumin Human (USP): Albumin human is a sterile nonpyrogenic preparation of serum albumin which is obtained by fractionating material (source blood, plasma, serum, or placenta) from healthy human donors. The source material is tested for the absence of hepatitis B surface antigen. It is made by a process that yields a product safe for intravenous use.

Albumin Solution, Human (PhEur): Human albumin solution is an aqueous solution of protein obtained from plasma. Separation of the albumin is carried out under controlled conditions so that the final product contains no less than 95% albumin. Human albumin solution is prepared as a concentrated solution containing 150-250 g/L of total protein or as an isotonic solution containing 36-50 g/L of total protein. A suitable stabilizer against the effects of heat such as sodium caprylate (sodium octanoate) or *N*-acetyltryptophan or a combination of these two, at a suitable concentration, may be added but no antimicrobial preservative is added at any stage during preparation. The solution is passed through a bacteria-retentive filter and distributed aseptically into sterile containers which are then closed so as to prevent contamination. The solution in its final container is heated to 60 ± 0.5°C and maintained at this temperature for not less than 10 hours. The containers are then incubated at 30-32°C for not less than 14 days or at 20-25°C for not less than 4 weeks and examined visually for evidence of microbial contamination.

14. Safety

Albumin occurs naturally in the body, comprising about 60% of all the plasma proteins. As an excipient, albumin is used primarily in parenteral formulations and is generally regarded as an essentially non-toxic and non-irritant material. Adverse reactions to albumin infusion rarely occur but include nausea, vomiting, increased salivation, chills, and febrile reactions. Urticaria and skin rash have been reported. Allergic reactions, including anaphylactic shock can occur. Albumin infusions are contraindicated in patients with severe anemia or cardiac failure. Albumin solutions with aluminum content of less than

200 µg/L should be used in dialysis patients and premature infants.⁽⁶⁾

15. Handling Precautions

Observe handling precautions appropriate for a biologically derived blood product.

16. Regulatory Acceptance

Included in the FDA Inactive Ingredients Guide (IV injections). Included in parenteral products licensed in the UK.

17. Pharmacopeias

Eur and US.

18. Related Substances

Albumins derived from animal sources are also commercially available, e.g., bovine serum albumin.

19. Comments

A 100 mL aqueous solution of albumin containing 25 g of serum albumin is osmotically equivalent to 500 mL of normal human plasma.

20. Specific References

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21. General References

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22. Authors

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